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How Do I Do It

Quantitative assessment of left ventricular systolic function using 3-dimensional echocardiography

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ABSTRACT

Assessment of left ventricular systolic function is the commonest and one of the most important indications for performance of echocardiography. It is important for prognostication, determination of treatment plan, for decisions related to expensive device therapies and for assessing response to treatment. The current methods based on two-dimensional echocardiography are not reliable, have high degree of inter-observer and intra-observer variability and are based on presumptions about the geometry of left ventricle (LV). Real-time three-dimensional echocardiography (RT3DE) on the other hand is fast, easy, accurate, relatively operator independent and is not based on any assumptions related to the shape of LV. Owing to these advantages, it is the Echocardiographic modality of choice for assessment of systolic function of the LV. We describe here a step by step approach to evaluation of LV volumes, ejection fraction, regional systolic function and Dyssynchrony analysis based on RT3DE. It has been well validated in clinical studies and is rapidly being incorporated in routine clinical practice.

1. Introduction

Assessment of left ventricular structure and function has been the most common indication for performance of echocardiography since the beginning of the field of echocardiography owing to its widespread availability and ease of use. The heart has been viewed primarily as a pumping organ and the assessment of the adequacy and efficiency of the contractile function of the heart has been considered as a prime marker of its disease. Studies done over the years have shown that evaluation of systolic function of the left ventricle (LV) is not only important for diagnosis, but is also a robust marker of overall prognosis and is critical to planning treatment in diverse clinical situations. For example, objective and accurate assessment of left ventricular ejection fraction (LVEF) is vital for selection of patients of heart failure who are suitable candidates for the expensive but effective device therapies (biventricular pacing and implantable defibrillators). The earlier methods of assessment of left ventricular size and systolic function (one and two dimensional echocardiography) are limited in scope since they are based on geometrical presumptions of LV shape, which is an extremely variable parameter, especially in presence of severe LV dysfunction. These methods are also time consuming, cumbersome and

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suffer from high degree of intra- and inter-observer variability. As a result of these limitations "Eyeballing method" evolved and was widely believed to be accurate but clearly is not acceptable in this day and age when important decisions are required to be made based on the accurate estimation of LV function. The current "gold standard", cardiac MRI, is expensive, not widely available and cannot be performed in sick patients and in patients with implanted pacemakers/defibrillators. Cardiac MRI is therefore not an option in day to day clinical practice for quantification of left ventricular systolic function.

Three dimensional echocardiography (3DE) has developed greatly during the last decade and it is now possible to perform real-time three-dimensional echocardiography (RT3DE) at the bedside, with the probes having small footprints and without the need of complex offline processing. Technological advancements in image acquisition and analysis have ensured that the 3D volume datasets of the LV can be acquired and analyzed for assessments of LV morphology and systolic function, with high degree of accuracy and reproducibility, noninvasively, at the bedside. Considering the need of accurately and reproducibly assessing the LV systolic function and widespread availability of 3DE, it is incumbent upon the cardiologists performing echocardiography to acquaint themselves with the technique of measuring LV systolic function using real-time three-dimensional echocardiography (RT3DE). The present article discusses the fundamentals of 3DE and then describes, in a stepwise approach, the methods of 3D image acquisition, analysis and interpretation, for assessment of global LV systolic function, regional systolic function and Dyssynchrony analysis.

2. 3D echocardiography

Real-time three-dimensional echocardiography (RT3DE) is performed using fully sampled matrix array transducers using micro beam forming technology.[1] This system allows incorporation of large number of piezoelectric crystals and their attendant circuitry in a small housing, which can be incorporated into the transthoracic or transesophageal probes. The same probe is used for performing 2D and Doppler echocardiography. As opposed to 2D echocardiography (2DE) where a narrow sector of image is formed, a 3D image is acquired in the form of a pyramid (often referred to as the "dataset") due to simultaneous firing of large number of crystals in space. Typically, 3D systems perform image acquisitions in several different formats or modes (Fig. 1). These are the live 3D, live 3D zoom mode, full volume mode and full volume color mode. All these modes are incorporated in the transthoracic as well as in the transesophageal probes and have specific utility.[2] The live 3D or narrow angle mode acquires a $50^\circ \times 30^\circ$ pyramidal dataset which can be viewed live. Since this is a narrow and small pyramidal dataset, it is useful for visualizing small structures like vegetations, small masses or small valves at a distance from the probe. It also offers very good spatial and temporal resolution. The zoom mode acquisition is similar to the 2D zoom application since it allows the operator to manually select a structure of interest and select it for viewing. It produces a smaller ($30^\circ \times 30^\circ$), high resolution, magnified pyramidal dataset which can be viewed live from different perspectives. The spatial and temporal resolution is less than in live 3D and full volume modes but it obviates the need for cropping and provides excellent real time images of the structure of interest (for e.g. mitral valve enface view using 3D TEE).

The full volume mode displays a wider angle ($90^\circ \times 90^\circ$) pyramidal dataset and is used to acquire the entire heart or the left ventricle. As opposed to the live 3D and zoom modes, this does not consist of a single volume but a number of subvolumes (typically four to seven), acquired over a corresponding number of cardiac cycles and stitched together. As such, the raw full volume dataset cannot be viewed live and looks unspectacular from outside. The pyramidal dataset thus obtained has to be acquired and then, using the software, subjected to "cropping" in any plane to select the structure to be viewed, and can also be rotated in any plane. One can also adjust the size of the dataset and number of subvolumes, before image acquisition. This mode offers as good a spatial and temporal resolution as seen with live 3D mode but the drawbacks of this mode are the stitch artifacts due to the translational motion of the heart owing to breathing and variation of cardiac cycles due to arrhythmia (atrial fibrillation). As such; it is advisable to acquire the full volume datasets during breath holding and with ECG gating. Besides, with the technological advancement, single beat echo may soon become a possibility which will overcome these problems.

Full volume color Doppler is also available for assessment of regurgitant lesions in both transthoracic and transesophageal probes.

3. 3D echocardiography for LV systolic function

Several different platforms are available for quantification of the left ventricular systolic function and broadly, all utilize the same basic principles of 3DE. The steps for quantification of LV systolic function are essentially similar in all the different software provided by these vendors.

3.1. *Image acquisition*

Good quality 3D imaging depends on good background 2D images. The patient should optimally be in the left lateral position and instructions about breath holding should be given well in advance.

- It is advisable to perform a comprehensive 2D and Doppler examination before starting the 3D examination. The 2D image should be optimized with adequate gain settings with both TGCs and LGCs being in the middle.
- High-quality ECG tracing should be visible on the monitor to enable ECG gating.
- Using the apical window, an apical 4 chamber view is formed avoiding foreshortening and ensuring that the entire LV is within the sector. The depth should be minimized to include only the mitral valve.
- Next, "live 3D" mode is selected to view the entire LV in 3D. Again, the gain settings and TGCs are adjusted to obtain

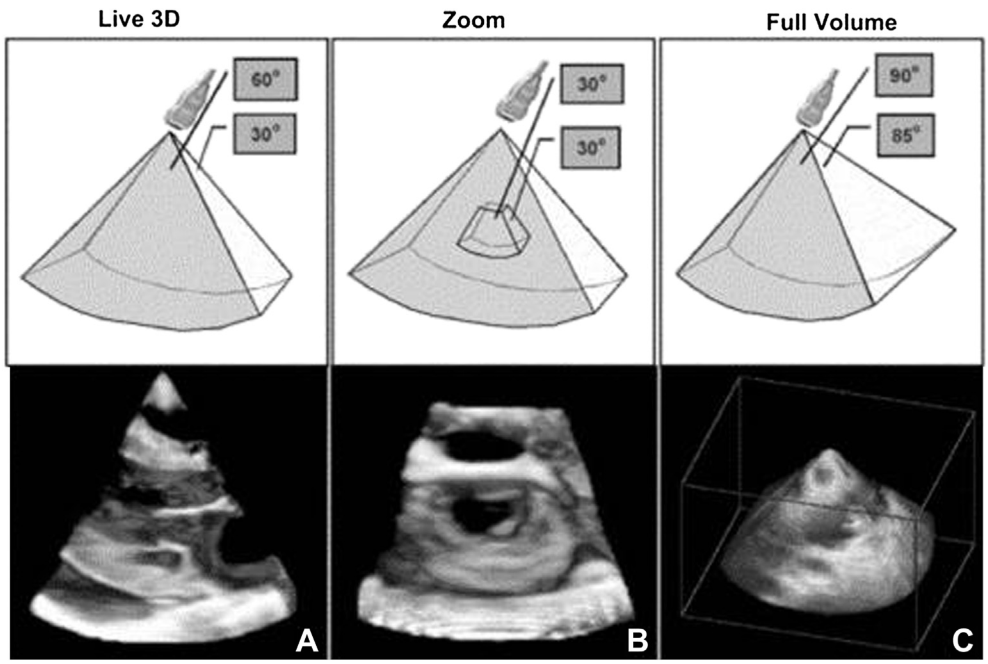

Fig. 1 – Modes of 3D echocardiography. J Am Coll Cardiol. November 21, 2006, 48 (10): 2053–2069.

optimal surface rendering. One can also select the color scheme in this view as most systems provide the option of choosing from a range of options.

- "Full volume" mode is then selected from the screen. This will provide LV in the form of a pyramidal dataset. Ensuring that the entire LV is visualized, avoiding all movement, the patient is asked to hold breath in end expiration and the dataset is acquired.
- Before acquisition, it is ensured that at least four cardiac cycles with regular R–R intervals are chosen for acquisition.

3.2. *Assessment of global LV systolic function*

The full volume dataset of the LV that has been acquired and stored can be subjected to offline analysis for assessment of LV volumes, systolic function and dyssynchrony. The analysis is possible either on the machine itself or, at a remote workstation having the appropriate software. The process of analysis is simple, rapid and accurate. It usually takes less than a minute to completely assess LV systolic function and it has a steep learning curve.

- The 3D quantification software is launched and the full volume dataset to be analyzed is opened in the software. The dataset is displayed as a series of stop frame images.
- The first stop frame image is generally the end-diastolic frame but it is advisable to scroll through the images and mark the end-diastolic and end-systolic frames.
- First, the end-diastolic frame is selected and it is ensured that the two long axis image planes are aligned exactly with the long axis of the LV to avoid foreshortening. This is one of the greatest advantages of the 3D over 2D imaging; hence it is very important to do it correctly (Fig. 2).
- Next, 5 points are marked to define the medial mitral annulus, lateral mitral annulus (in the 4 chamber plane), anterior and inferior mitral annulus (in the 2 chamber plane) and the apex (in either plane).
- Medio-lateral alignment and orientation for correct identification of LV segments are provided by selecting the arrow in the short axis plane and pointing it towards the middle part of interventricular septum (Fig. 2).
- The system automatically tracks the complete LV endocardial border using this information and generates a volumetric end diastolic cast of the left ventricle with the end diastolic volume displayed on the screen. It is also possible to manually correct the endocardial tracing but the semi-automatic approach is fairly accurate and manual adjustment should be kept to the minimum (Fig. 3).
- End systolic frame marked earlier is selected and the same 5 points are marked in the long axis planes. This generates the end systolic volume and the ejection fraction.
- After tracking of the endocardial borders in the 3D dataset for each acquired time frame, a global time versus volume curve is generated displaying the dynamic change in the LV volume over the entire cardiac cycle. The lowest point represents the end systolic volume, while the maximum being the end diastolic volume (Fig. 4).

3.3. *Assessment of LV mass*

RT3DE can also be used for non-invasive measurement of LV mass. It is based on the principle of measurement of LV myocardial volume and multiplying it with myocardial density (1.04 g/ml). LV myocardial volume is derived by subtracting the LV cavity volume (by tracing out the endocardial border) from LV epicardial volume (by tracing out the LV epicardial border). Both these measurements are obtained in the end-diastolic frame. The biggest advantage of 3D derived LV mass is that it avoids foreshortening of the LV, which is almost impossible to ensure with 1D and 2D

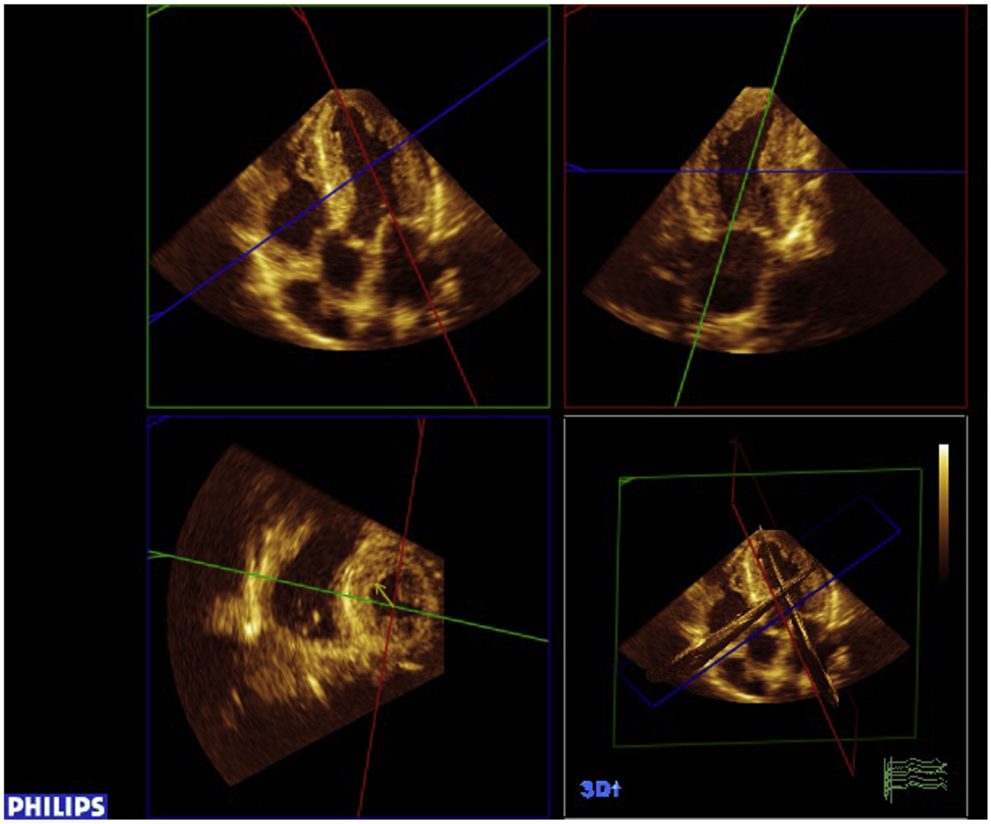

Fig. 2 – **Proper alignment of the two long axis 2D planes of the left ventricle as indicated by the red and green lines. This ensures that true long axis of the left ventricle is identified. The yellow arrow is aligned to point towards mid part of interventricular septum for proper orientation.**

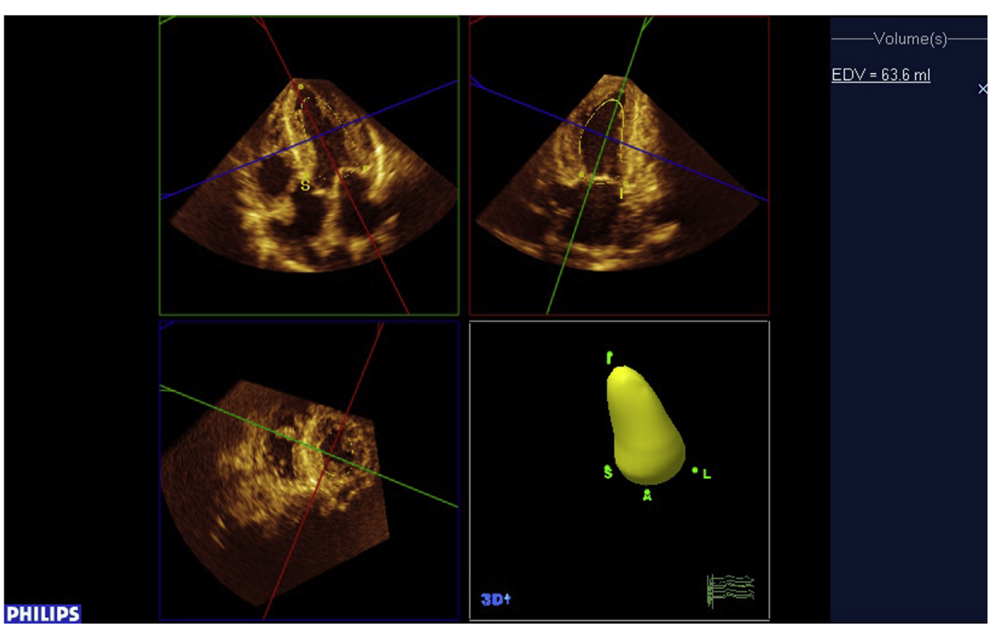

Fig. 3 – **The top two quadrants show the marking of 5 points-medial mitral annulus, lateral mitral annulus, apex (in the first quadrant), anterior and inferior mitral annulus (in the second quadrant). Semiautomatic endocardial border detection is shown by yellow line and the lower right quadrant shows the LV end diastolic cast. The end diastolic volume is depicted on the right.**

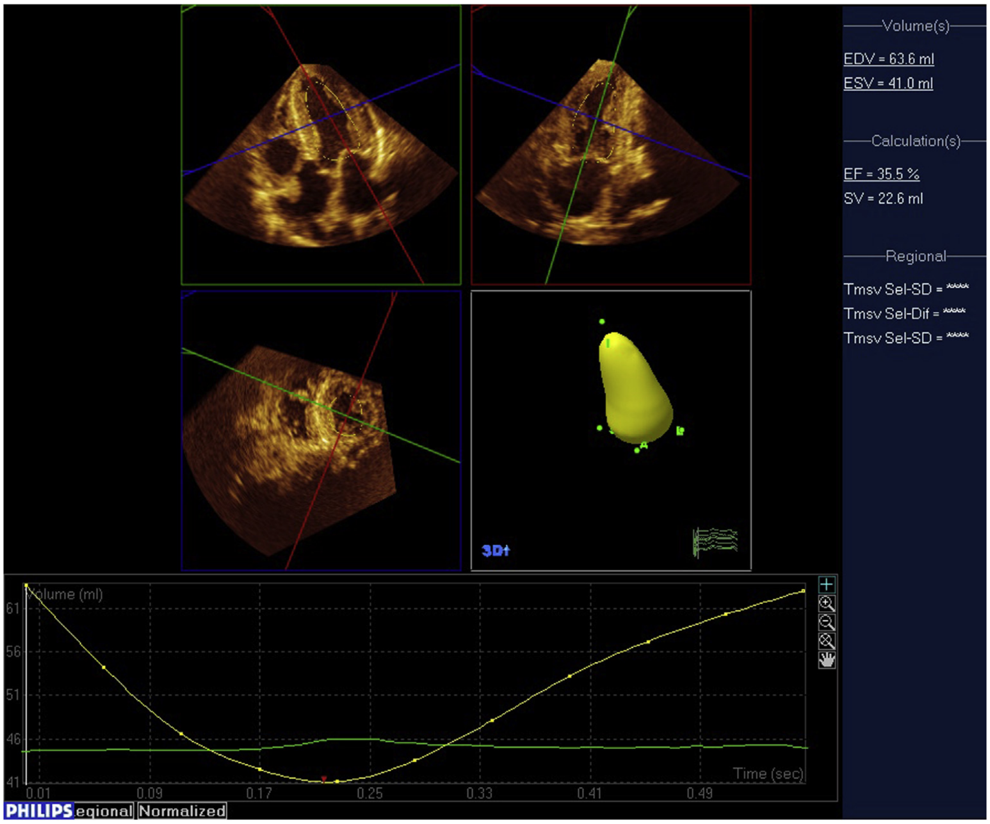

Fig. 4 – End systolic frame with end systolic volume, stroke volume and ejection fraction calculated by 3D. The lower panel shows global volume time curve for LV.

echocardiography methods. Tracing out the epicardial border in the acquired full volume dataset is however, a bit challenging compared to volume measurements, as done above.

Once the borders have been traced in the end diastolic frame, the machine automatically calculates LV mass based on the formula below and displays the value on the screen (Fig. 8).

(3D LV Mass = (Epi – vol) – (Endo – vol) × Myocardial density)

3.4. *Assessment of regional LV systolic function*

Using RT3DE, regional LV function can be analyzed by three methods. This is possible since the full volume dataset contains complete dynamic information of the left ventricle during one cardiac cycle.

- In the first method called the *long axis method*, the full volume dataset can be sliced in any longitudinal plane and the various segments (defined by the American Society of Echocardiography), can be visually studied for contractile function. Though it is a subjective approach, this method is more accurate than eyeballing by 2D method because the errors arising due to incorrect plane and foreshortening are avoided by the 3D method. The thick slices created by 3D slicing or cropping contain more tissue information as compared to the 2D generated thin slices.
- In *multiple slice technique*, the entire LV is divided into a stack of short axis views and displayed on the screen (Fig. 5). It is well known that visualizing the circumferential shortening is a more sensitive technique as compared to the long axis planes for detection of subtle wall motion abnormalities. This tomographic approach is identical to the one used in cardiac MRI for this purpose and is likely to be useful in stress echocardiography using RT3DE.
- In the *objective method* of regional LV systolic function, the full volume dataset acquired is subjected to semiautomatic endocardial edge detection after placing the landmark points as described above to obtain the global LV function data. By selecting the regional function option, the LV is automatically subdivided into 16 segments (as proposed by the ASE). Each of these volume segments is coded with a different color and volume–time curves displaying the maximum and minimum volume of each segment during the cardiac cycle is displayed. Based on the pattern of the curves, hypo contractile or no contractile segments can be easily identified as flat curves (Fig. 6).

3.5. *Assessment of LV Dyssynchrony*

- The regional function curves obtained above can be used to look for the presence of intraventricular Dyssynchrony in patients who have severe LV systolic dysfunction (LVEF 30–35%) and wide QRS complex on ECG. Based on the regional time–volume curves over the period of a cardiac cycle, a systolic Dyssynchrony index (SDI) is calculated of the 16 segments of the LV. The SDI is a measure of the

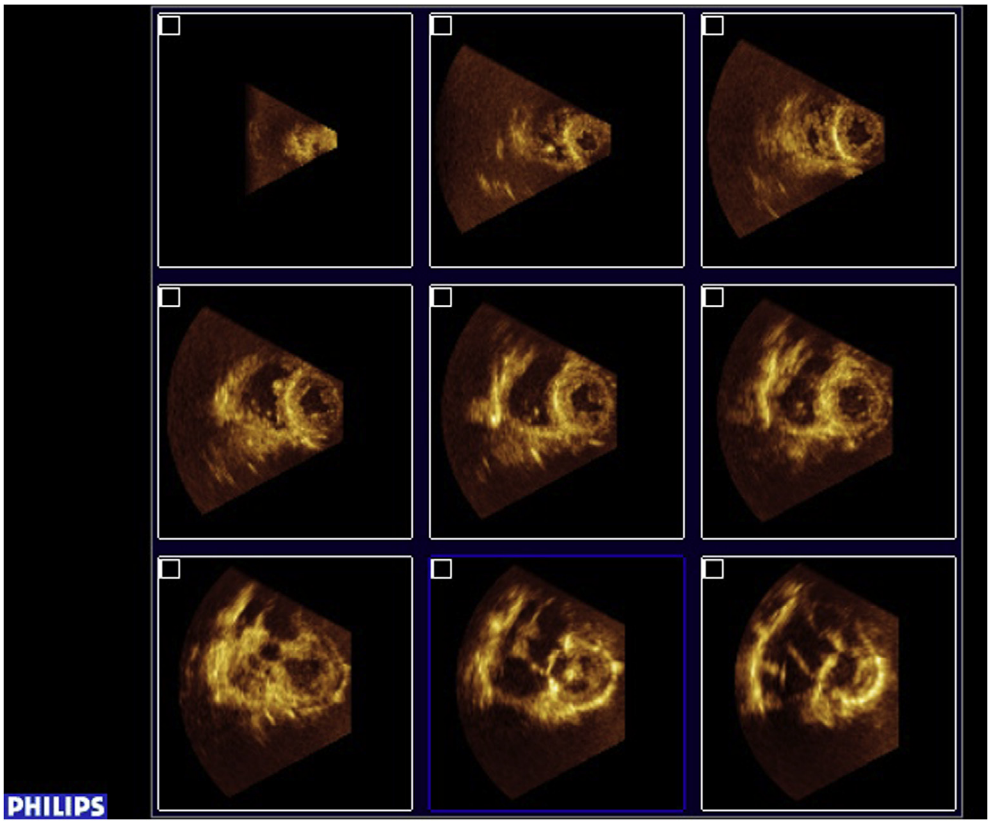

Fig. 5 – Short-axis views of the left ventricle at different levels oriented perpendicular to the long axis. There is an option of selecting the thickness and the number of slices in some of the softwares.

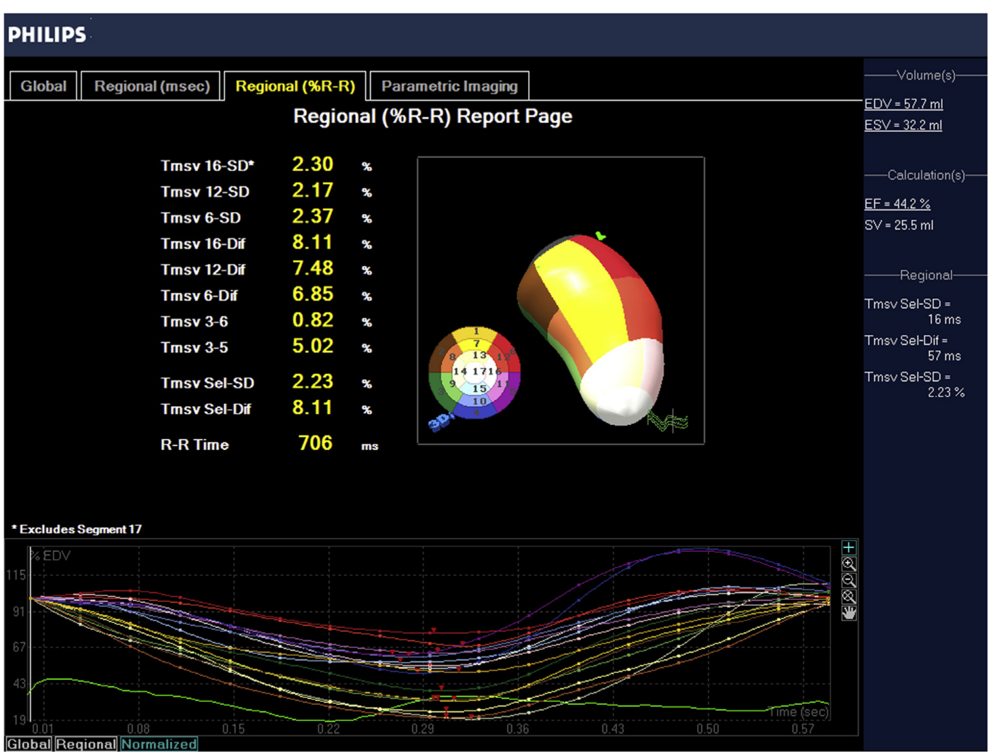

Fig. 6 – Three dimensional regional-LV analysis with segmental time volume curves. The numbers denote the standard deviations of time to maximal velocity (Tmsv) for different selection of segments. The Tmsv 16-SD value of 2.3 denotes normal synchrony.

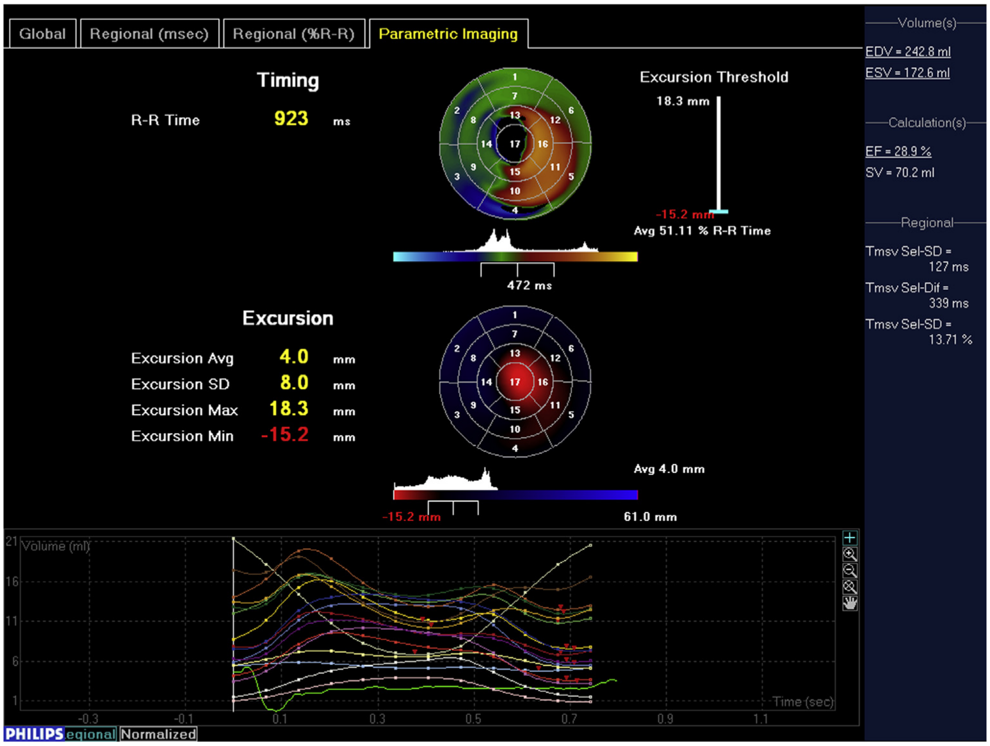

Fig. 7 – Parametric image display of segmental timing (above) and excursion (below) in a patient with dilated cardiomyopathy. In the upper map, the segments in red (posterolateral) are shown in red, while the segments in blue are contracting early. In the lower map, segments in red denote dyskinetic segments (apex and posterolateral segments). In the bottom of the picture are seen the segmental time volume curves.

standard deviation of the time to maximal velocity of all the 16 segments of the LV and is displayed on the screen as Tmsv 16-SD (Fig. 6).

- Another subjective method of Dyssynchrony is to select any two opposing segments and find the difference in their time to maximal velocity. Differences in time to peak velocity of any two segments or even all the segments of opposing walls can be selected and displayed.

The greatest advantage of 3D based calculation of Dyssynchrony is that all the segments are displayed in the same cardiac cycle as opposed to the 2D and Doppler methods where it is not possible to view and calculate the time to peak velocity of myocardial segments in the same cardiac cycle, simultaneously.

4. Parametric image display

RT3DE offers the unique possibility of visualizing the entire LV as a whole with large amount of special and temporal information. Displaying only the regional segmental information in the form of regional velocity–time curves misses out a large amount of information about the rest of endocardium. Some 3D platforms offer the parametric display option wherein the endocardium is sampled at more than 800 points and the information displayed as a polar map of the entire LV endocardium. Regional endocardial motion is displayed based on the information derived by the movements of these points from end-diastole to end-systole and displayed as a color coded plot superimposed on the 17 segments proposed by the ASE. Normal inward motion is displayed in varying shades of blue while out ward motion by shades of red. Akinetic segments are displayed as black. Thus, a normokinetic segment will appear as dark blue, a hypokinetic segment as light blue and a dyskinetic segment will appear in shades of red. This polar map gives instant information about the overall distribution and extent of regional wall motion abnormalities for the entire LV (Fig. 7).

Apart from displaying the *extent* of endocardial excursion, it is also possible to display the *timing* of excursion of the different segments of the entire LV endocardium in the form of a parametric image. The time to maximal excursion for each segment, is displayed as a color coded polar map. Average time to maximal excursion is displayed as green; excursions occurring before the average time are displayed in shades of blue while the events occurring after the average time are displayed in shades of red. In a synchronous ventricle therefore, all the segments will be displayed in green while in presence of LBBB, the early contraction of the septum will be seen in blue while the late moving antero-lateral segments will be seen in red (Fig. 7).

Different vendors may offer different color schemes and different display patterns but the overall information provided is the same. For example, particular software offers the possibility of viewing the parametric display in the form of a moving image over the entire cardiac cycle (contraction front mapping) to enhance the overall visual impact of events.

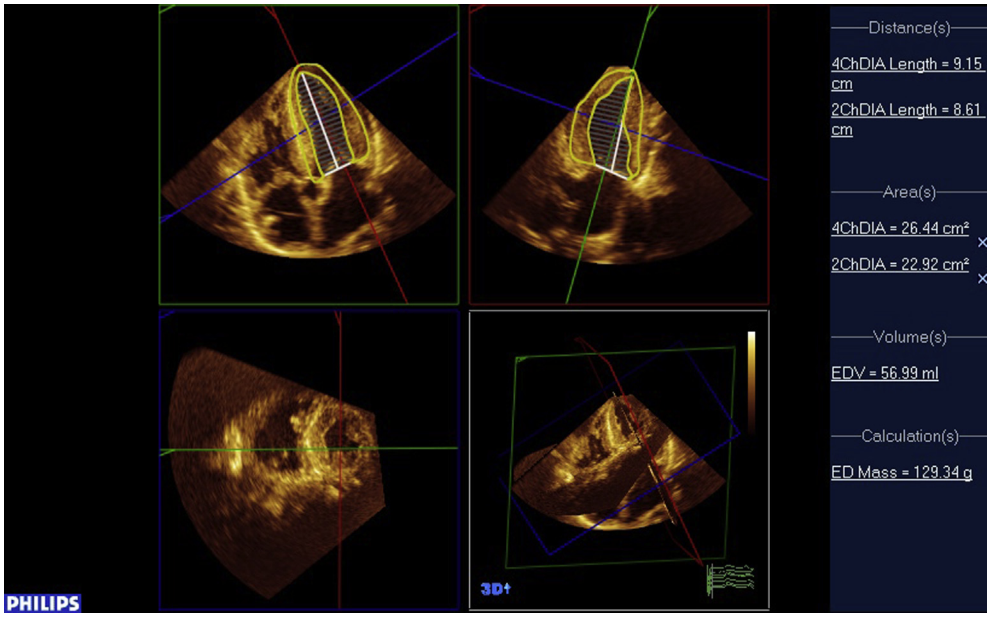

Fig. 8 – Endocardial and epicardial borders are traced in the end-diastolic frame in the 4 and 2 chamber views (upper left and right boxes). The LV mass is displayed automatically on the right side of image.

5. Clinical utility of 3D evaluation of LV systolic function

As discussed earlier, evaluation of global LV systolic function using LVEF as the index is the commonest indication for performing echocardiography. Although, it is a load dependent parameter, accurate estimation of LVEF is relied upon for major treatment decisions and prognostication. 3DE calculates LVEF without any geometrical assumptions, which is a major limitation of 2DE.[3] Studies have clearly shown that the actual geometry of the LV in disease states is much different than what it is presumed while calculating LVEF using 2DE.[4] Therefore volumetric calculations by 2DE are incorrect in severe disease states of the left ventricle.[5] Another major limitation of the 2D methods is poor reproducibility since it depends on accurate placement and positioning of the thin cut plane in the 2D, from study to study which is not possible.[6] Several studies have now clearly demonstrated that 3DE is more accurate and reproducible for calculation of LV volume and ejection fraction, even in severely diseased left ventricles with distorted geometries.[7–9] Since 3D technique is based on semiautomatic border detection with very little interference from the operator, it is fast, easy and relatively observer independent with a steep learning curve.[10] The 3D approach has been validated using cardiac MRI, the current gold standard for calculation of LV volumes and ejection fraction.[11,12] The greater reliability and reproducibility also makes 3D as the method of choice for serial evaluation of LVEF[13] and for choosing expensive device therapies in patients with severe LV dysfunction. A small study has also indicated that LV volume estimation by RT3DE also has prognostic value in patients with acute myocardial infarction.[14]

Assessment of regional myocardial function using 3D echocardiography and depiction of contractile function in the form of time–volume curve has been validated against cardiac MRI.[15] It is a very objective, reproducible and reliable method of assessment of regional LV function as compared to "eyeballing" by 2DE.

Cardiac resynchronization therapy (CRT) is an established therapy for patients with severe LV dysfunction, refractory to medical therapy with LBBB. However, there is a uniform nonresponder rate of around 30% in spite of CRT. Conventional echocardiography and novel techniques like tissue Doppler echocardiography have consistently failed to identify likely predictors of CRT.[16] Since RT3DE evaluates the complete LV in real time and offers the advantage of simultaneously comparing the segmental excursions, it is likely to be more accurate in assessing regional Dyssynchrony. 3D derived systolic Dyssynchrony index (SDI) has been studied and found to be a robust marker of regional Dyssynchrony and predictor of response to CRT.[17,18]

RT3DE derived LV mass has been compared to 1D and 2D echocardiography methods using cardiac MRI as the gold standard and has been found to be more accurate.[19,20]

6. Future perspective

RT3DE has rapidly become popular and is now widely available since its beginning, about a decade ago. RT3DE has now being incorporated into TEE probes with a small footprint. Many vendors are now offering simple, easy to use applications where quantitative processing of the 3D dataset can be performed either on the machine itself or at a separate location. A major limitation for full volume assessment is the need of breath holding during acquisition and requirement of sinus rhythm to avoid stitch artifacts. In sick patients, on ventilator, and with arrhythmia, this becomes a problem. The development of single beat echo is likely to overcome this problem in the future. Also, since 3DE requires good quality 2D imaging in the background, patients with poor acoustic window have poor transthoracic 3D datasets with endocardial dropouts resulting in incorrect assessment of LV volume and EF. However, with the ease of use, accuracy, reproducibility and availability, RT3DE has already become the echocardiographic modality of choice for evaluation of left ventricular systolic function.

Conflicts of interest

All authors have none to declare.

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